Abstracts from the Second International Hidradenitis Suppurativa Research Symposium
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Which HS key issues remain unanswered?

Viewpoint: Two Key Issues
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There are two key issues to address:
• The contradiction between anatomical locations of the disease (i.e. apocrine zones) and the histological features of absence of early involvement of apocrine glands. There is a paucity of data on physiology and pathology of apocrine glands. One of the main challenges is to identify the specificity of the apocrine follicle in HS.
• HS is an auto-inflammatory disease presumably related to alteration in innate immunity in the apocrine follicle. Identification of the specific defect in the TLR-cytokine network should be priority in investigation.

Viewpoint: Where should we look for Hidradenitis suppurativa?
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The typical histology of hidradenitis suppurativa is the formation of sinus tracts in the dermis and the subcutis, similar to the formation of inflammation due to a foreign body. Biologically, the cells represent a poorly understood phenomenon involving the infiltrative growth of proliferating non-malignant stem cell like keratinocytes. It is likely that the stem cell like cells emerge due to the influence of unknown local factors. Sinus tract formation may represent an aberrant epidermal repair response executed by activated keratinocytes. The processes progress until the recurring abscesses reach a critical size. The complex of fibroblasts-angiogenenic cells-keratinocytes-inflammatory cells spills on to the surface during expansion. At a point of equilibrium, the hyperactive abscess turns into a draining sinus followed by non-malignant/pseudo-malignant infiltrative growth in the dermis and subcutis.

Viewpoint: Through the “hair follicle lens”
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In a recent “Controversies” feature (Kurzen et al., Exp Dermatol 17:455-72, 2008), some of the pertinent open questions on the pathobiology of HS have been summarized. These include e.g.:
• If HS primarily is a chronic inflammatory disorder of the hair follicle epithelium, but not of the apocrine gland, why does it preferentially occur in intertriginous skin rich in apocrine glands?
• Why after puberty, and in more women than men? What is the genetic and (neuro-)endocrine basis of this?
• What are the initial triggers of follicular occlusion and its tissue-destructive, inflammatory sequelae? Namely, is bacterial superinfection only a secondary event, or are bacterial products already involved in the excessive stimulation of innate immunity signals (e.g. release of antimicrobial peptides and chemokines) from the distal hair follicle epithelium that we have hypothesized to be crucial in HS pathobiology?
• Which compartment of the hair follicle epithelium exactly is the very first “nucleus of HS pathogenesis” (e.g., the periinfundibular, distal outer root sheath [ORS]?)
• Is the hyperkeratosis and hyperproliferation of distal ORS keratinocytes one sees early during HS pathogenesis a primary event, or only a consequence of prior inflammatory stimuli?
• How does the hair follicle innate immune system in as yet uninvolved intertriginous skin of HS patients differ from that of normal controls?
• What exactly is the role of nicotinergic acetyl choline receptors in HS pathobiology?

These selected open questions will be discussed on the basis of recent insights into hair follicle immunology and hair follicle neuroendocrinology.

Histopathology of “hidradenitis suppurativa” alias acne inversa
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The term “hidradenitis suppurativa” is firmly entrenched in the dermatological literature although it refers to a false pathogenetic concept. The term was historically coined based merely on the characteristic distribution of the apocrine glands and the anatomical coincidence with the disease process. The hereinafter histopathological analysis of 176 specimens of “hidradenitis suppurativa” from 152 patients found at the center stage of the disease not a suppurative inflammation of the apocrine sweat glands but an occlusion of the hair follicles, comparable to acne vulgaris.

The disease process starts with follicular hyperkeratosis and dilatation of the follicular infundibula evolving into comedones, comparable to the ones observed in acne vulgaris. At this time, the apocrine glands are not involved. Eventually the dilated follicular infundibulum ruptures and the content spills into the surrounding dermis, evoking an acute inflammatory response in the immediate vicinity of the rupture site. Again, the apocrine glands do not show any signs of involvement nor an indication that they are the anatomical starting point of the sequence of events. If the inflammation remains confined to the immediate vicinity of the hair follicle, over time the initially neutrophilic infiltrate subsides and is gradually replaced by a granulomatous one, often with the addition of multinucleated foreign body giant cells. If, however, the acute inflammatory response following rupture is more florid, a large abscess develops which may extend into the subcutaneous tissue. Apocrine glands near the abscess but not involved by it, are unremarkable. Only by extension of the inflammatory process, apocrinitis evolves and apocrine glands are destroyed. Apocrine glands located further away from the extending abscess are morphologically unremarkable. When extensive tissue destruction has ensued, naked hair shafts, surrounded by an inflammatory infiltrate, are often the only indication that the process started from the hair follicle. In an attempt of the tissue to confine the inflammatory reaction and to prevent further spread, remnants of the hair follicle epithelium proliferate and sinus tracts form, often surrounded by fibrosis. The sinus tracts communicate with the surface. Upon bacterial superinfection, they rupture and the process becomes self-maintaining and enters into a vicious cycle. Sinus tract formation is the main reason for the chronicity of the disease and why radical surgery is the only therapeutic option capable of achieving long-lasting cure.

Thus, “hidradenitis suppurativa” is a disorder that shares histopathological and clinical aspects with acne vulgaris modified under the special circumstances of anatomical regions rich in apocrine glands. It is acne inversa because in contrast to acne vulgaris the disease involves intertriginous localizations and not the regions classically affected by acne.

Autoimmune mechanisms in the pathogenesis of HS
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There is accumulating body of evidence suggesting that patients with HS have severe derangements of their innate immune system. This evidence is based on monocyte stimulation assays and on the favorable clinical responses with biological therapies.

Blood monocytes were isolated from 53 patients and stimulated with lipopolysaccharide (LPS) of Escherichia coli O144:H4 (1). Defective monocyte responses characterized by reduced production of tumor necrosis factor-alpha (TNF_α) and interleukin-6 (IL-6) were found. In the same study, it was shown that NK cells of patients were increased. These findings pointing towards serious derangements of the innate immune responses in the event of HS, led to a prospective, open-label, one arm clinical trial of the administration of etanercept in 10 patients with HS (NCT00329823, www.clinicaltrials.gov) (2). Etanercept was administered at a dose of 50 mg sc once weekly for 12 weeks. Efficacy of treatment was evaluated by the Sartorius score and by the disease activity index. A more than 50% decrease of both
scores compared with baseline was found in seven patients. All patients reported decrease of pain by week 4 whereas the number of fistulas was significantly decreased. Treatment was well-tolerated. Relapse was noted within 4-8 weeks after cessation of therapy.

The above findings implicate derangements of the innate immune system as part of the mechanism of pathogenesis of HS. They also point towards autoimmunity as part of its etiology.

References


Hidradenitis suppurativa and bacteria

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HS has been viewed as an infectious disease in the past and antibiotic therapy has been the most frequently recommended therapy. Recent studies, however, have failed to recover pathogenic bacteria in most cases. Our studies also show that recovery of pathogenic bacteria such as S.aureus, Pseudomonas etc., is uncommon. A recent study reports success with high dose clindamycin. This study has been confirmed in an open trial. These results indicate the need for prospective, controlled studies with high dose clindamycin with anaerobic cultures.

Cytokine production by mononuclear cells induced by clinical isolates of *P. acnes* bacteria

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Acne vulgaris is a multifactorial inflammatory disease of the sebaceous follicles of the face that frequently occurs in adolescence. Initially, acne starts as a non-inflammatory comedo. Subsequently, inflammatory reactions evolve to pustules, granulomas and cystic lesions. Many pathogenic mechanisms have been proposed including sebum excretion, obstruction of hair follicles, impaired keratinization of hair epithelium, bacterial overgrowth and immunological mechanisms; the role of *Propionibacterium acnes* (*P. acnes*) is particularly important. However, the host immune response to *P. acnes* has not been as yet elucidated. The aim of the present study is to evaluate the importance of the immune response to *P. acnes* and the bacteriological factor in the pathogenesis of acne. *P. acnes* isolated from acne lesions and healthy volunteers skin were cultured. The peripheral blood mononuclear cells (PBMC) from acne patients or healthy volunteers were stimulated with viable *P. acnes*, and cytokine production was evaluated using RT-PCR and ELISA. IFN-γ, IL-12p40, and IL-8 mRNA and protein production were significantly increased in PBMC from acne patients compared to that from normal donors. However, different *P. acnes* species isolated from acne lesions or normal subjects showed no difference in cytokines production from acne patients and normal subjects PBMC. The inflammatory response of acne appears to be attributable to *P. acnes*-induced host immune response rather than *P. acnes* strains from normal skin and acne lesions.

Genetics of Hidradenitis Suppurativa

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Hidradenitis suppurativa (HS), also known as Acne inversa is a chronic, inflammatory, painful, skin condition, characterized by swollen or inflamed lesions on the groin, anogenital parts, buttocks, thighs, scalp, neck, nipples, and armpits, with subsequent scarring and chronic seepage. Its incidence ranges from 1 in 100 to 1 in 600 with the age of onset from 25-35 years. Since 1839, scientific literature was
documented on family-based studies of HS. HS can occur as an isolated genetic anomaly or in association with over two dozen best known syndromes. We have studied nine families with multiple anomalies fitting with OMIM 142690, the gene of which is at present unknown. The expression of the phenotype was variable and ranged from moderate to severe. The mode of inheritance appears to be autosomal dominant with full penetrance. There were also two consanguineous marriages observed in one multigenerational pedigree (UR252) of Arab origin. Candidate loci for the described phenotype include on chromosome 1p21.1-1q25.3. Two-point linkage analysis and haplotype data did not show the involvement of the above region in our two studied families. Genome-wide linkage analysis is in progress to map the elusive locus and provide a target for positional cloning. A detailed data of the current state of genetic and phenotypic studies of HS will be presented.

Workshop: HS Teaching Module for Physicians
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Hidradenitis suppurativa (HS) is a poorly recognized condition that affects 1% of the population. For decades patients have had the diagnosis missed, usually incorrectly diagnosed as recurrent “boils”, resulting in poor care. They suffer from undiagnosed symptoms, waste millions of dollars on antibiotics, hide from society, endure pain and dysfunction and are desperate for help. There is a serious lack of knowledge about this condition amongst physicians, surgeons and medical caregivers. This workshop is being presented in an effort to remedy this problem.

Accurate diagnosis is the cornerstone of hidradenitis suppurativa care. Information on diagnosis and management must be easily available to practitioners. It is important to develop accessible and useable information with appropriate links to references and other relevant sites. Patient education is highly important. It will be helpful to provide them with forms for self-referral to caregivers. An HS intake form has been developed and can be completed by patients before they see the caregivers, to provide details of their background for optimal HS management. A PowerPoint teaching program on HS has been developed and will be presented. Ultimately a management form will be developed after discussion at this meeting.

Ideally a website will contain easily accessible and useable HS information for patients and physicians and other caregivers, with appropriate links and forms for self-referral, patient intake and management with instructional cases.

Efforts will be made to designate educators for educational outreach to medical schools, postgraduate training programs and national organizations representing physicians’ assistants and nurse practitioners as well as family physicians and Emergency Department physicians to improve diagnosis and management of this difficult condition.

Workshop: Unroofing as a Surgical Method for HS
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The accepted and traditional surgical management of hidradenitis suppurativa consists of en bloc excisions of all tissue assessed as ‘involved’, followed by repair using primary closure (with or without flap coverage), grafting (usually with a fenestrated allograft), or healing by secondary intent. This is usually limited to Hurley Stage III disease. Incision and drainage in Hurley Stages I and II as a definitive technique is not acceptable and may be counterproductive.

There is a need for a technique for the middle ground between the occasional inflamed nodules of Stage I and the advanced subcutaneous, branching and epithelialized sinus tracks of Stage III.

Unroofing of inflamed lesions that are unresponsive to conservative management is best done early to minimize lateral spread of the process. The apparent continuous growth of appendageal epithelium beneath the epidermal surface, as the body attempts vainly to reconstitute the normal anatomy of the pilosebaceous and apocrine complex, provides continuous and increasing amounts of epidermal-sourced antigen. If one accepts the fact that the innate immune system is the prime mover in hidradenitis suppurativa, then the logical strategy is to remove entirely the antigen-bearing material, thus allowing the innate immune inflammation to cool, and permitting healing from below, avoiding the trapping of material beneath the surface.

Given that the above works well in the large hospital-based excisions and subsequent healing done in Stage III, it is suggested that the same technique, used on a smaller office-based scale, will provide a successful adjunct to medical therapy in Stages I and II and, especially when combined with aggressive hormonal and dietary management, will prevent the progression to Stage III that presents such a challenge to patient and physician (and surgeon) alike.
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The techniques are not technically difficult, can be performed in the office setting under local anaesthesia, require only simple post-op dressing care, and spare the patient the cost of hospital or ambulatory surgical center care, the morbidity of graft donor sites, the risk of dehiscence, the risk of deep infection, the risk of burying pathology and the risk of extending the process to the next Hurley Stage.

Several illustrative cases with intra-operative and post-op photos will be presented.

Workshop: Organizing an HS Specialty Clinic
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Since January 2006, the dermatology department of the University of Pennsylvania has staffed a dedicated clinic for hidradenitis suppurativa. The clinic has grown significantly from a resident run clinic to become a regional referral center. We will share our modest experience, some growing pains, and maybe even some insights into how to better serve these patients.

Clinical and diagnostic guidelines for HS
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Hidradenitis suppurativa (HS) is a chronic recurrent disease causing inflammation, suppuration and scarring of inverse areas. In the classic Hurley clinical grading system, stage I consists of one or more abscesses with no sinus tract or cicatriziation, stage II consists of one or more widely separated recurrent abscesses with a tract or scarring. The most severe cases, stage III, have multiple interconnected tracts and abscesses throughout the entire affected area.

Among HS patients seeking help from dermatologists for their disease, cases graded as Hurley II form the majority, and within this common disease stage group there is a wide variation of clinical findings and symptoms. Milder cases with comparatively small problems exist in this group, while the more severe cases may have debilitating symptoms. It is therefore important to develop a more dynamic and precise scoring system for HS by adding clinical details to the staging process. It is proposed that the following outcome variables are explicitly mentioned in future reports:

1. Anatomical region involved.
2. Number and scores of lesions (nodules and fistules).
3. The longest distance between two relevant lesions.
4. Are all lesions clearly separated by normal skin (Hurley stage III - yes or no)?

By assigning numerical scores to these variables, disease intensity can be quantified in a more clinically meaningful way on an open-ended scale. Furthermore, as pain is an important feature of HS a subjective evaluation should be included, preferably a visual analogue scale score of pain from the worst lesion, as chosen by the patient.

Associated (risk) and severity factors for HS
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Conflicting opinions have been reported regarding the epidemiology of hidradenitis suppurativa. We sought to evaluate its prevalence and to identify associated factors through a cross sectional study. Prevalence was evaluated using a representative sample of the French population (n =10,000). Associated factors were assessed using two case-control studies, one population-based with 67 self-reported patients and 200 control subjects, and the other clinic-based with 302 medically assessed patients and 906 control subjects.

The prevalence was 1% of the French population. Multivariate analyses showed a strong association with current smoking in self-reported (odds ratio = 4.16; 95% confidence interval [2.99-8.69]) and in medically assessed (odds ratio = 12.55 [8.58-18.38]) populations. Association with body mass index was significant in medically assessed patients (odds ratio = 1.12 [1.08-1.15]) for each increase of 1 U of BMI. These identified factors cannot be called “risk factors” as a causal relationship could not be established with such a cross-sectional study.
Factors associated with severity of hidradenitis suppurativa (HS) are not known. A series of 302 consecutive patients with HS were interviewed for associated factors and examined by a single investigator to evaluate severity using Sartorius score. In multivariable analysis, increase of body mass index (BMI), atypical localisations, personal history of acne, and absence of family history of HS were associated with a high Sartorius score.

Our data suggest that obesity, the presence of an atypical localisation, a personal history of acne and the absence of family history of HS are independently associated with severity of HS. Although Sartorius’ score is not formally validated it has been shown to be highly correlated to intensity and duration of pain and suppuration and to quality of life. Sartorius score is the best available outcome measure today.

The impact of hidradenitis suppurativa on quality of life
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Hidradenitis suppurativa (HS) is a chronically relapsing skin disorder. Affected patients suffer a significant morbidity and it is self evident that HS has a significant impact upon quality of life (QoL). Many dermatologists rate HS as a ‘heart-sink condition’ and would agree that it ranks among the most unpleasant skin diseases. When looking at the statement of patients about their disease they emphasize that the soreness and pain are the cause of their disability. Patients suffer of embarrassment and self-consciousness caused by the frequent occurrence of boils with malodorous discharge. In France, in the context of a TNS Sofres survey, which is deemed to provide a representative sample of patients with HS, about half the patients reported HS to be a relevant problem and a severe distress. Two studies using standardized QoL questionnaires were published in the literature (1, 2). QoL questionnaires were well tolerated by patients and allowed to evaluate the burden of HS and to compare it with other diseases. They demonstrated that the impact of HS is probably the highest encountered in chronic diseases in dermatology. These results are important for the recognition of the disease and the lobbying of lay groups. These questionnaires should be used for follow-up and therapeutic trials to take into account the viewpoint of patients.

The analysis of QoL measures confirmed the strong impact of HS. A subgroup of patients seemed to be more affected: patients with an early onset of their disease, with long disease duration, with continuous evolution and with predominating pelvic location. Future trials should be targeted on this subgroup. The impact upon QoL is strongly correlated with pain. Therefore criteria of treatment evaluation should include, in addition to the standardized report by the physicians, the viewpoint of patients collected with at least a dermatological QoL questionnaire and the visual analog scale for pain.

References

The psychological consequences of HS and their management
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It is well recognised by patients and their physicians that HS has a significant impact on the psyche, although data are limited. It has been shown that quality of life is reduced in both Danish and French patients, but specific psychological investigations are lacking. In addition, the methods used to describe the psychological impact are often qualitative rather than quantitative providing a relative barrier to the dissemination of information.

Six HS patients were therefore interviewed in exploratory single interviews to identify main topics in the psychological impact of the disease. After transcription and analysis, an additional four HS patients were interviewed in a focus group session to establish the validity of the claims.

A number of common dermatological problems were identified, but additional specific problems of social isolation due to smell were prominent in the patients’ perception of HS.

Data will be presented which may form the basis of disease specific quality of life questionnaires that may help a qualitative analysis of the psychology of HS in the future.
New Therapeutic Options for Hidradenitis suppurativa/Acne inversa (HS)
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Treatment of HS is often disappointing, and has significant negative impact on the patient’s quality of life. In an evidence-based analysis of standard treatments and recent advances in the therapy of HS, only treatment with topical clindamycin 1% solution, oral clindamycin and rifampicin or with the hormonal antiandrogen cyproterone acetate 100 mg/d achieved an evidence level 2 and a recommendation grade B. In a retrospective study, 14 HS patients have received clindamycin 300 mg 2x/d and rifampicin 300 mg 2x/d for 12 wk. Eight experienced complete remission of HS of 1-4 years after one course of treatment, and further two patients achieved remission after substituting clindamycin with minocycline (100 mg/d) because of transient diarrhoea. Four patients were unable to complete the course of treatment because of diarrhoea. The 10 responders have not subsequently relapsed.

In a pilot study, 22 patients with Hurley’s grade I and II were treated with 90 mg/d zinc gluconate. 8 complete remissions (CR) and 14 partial remissions were observed. When CR was obtained, the treatment was progressively decreased. 4/22 patients experienced side-effects, mainly gastro-intestinal.

In a retrospective study with 64 female HS patients, antiandrogen therapy was superior to oral antibiotic therapy (55% vs 26%). Female patients presenting with HS should prompt investigations for underlying PCOS and insulin resistance.

Intramuscular human immunoglobulin (HIG; 1320 – 1980 mg sc/m) administered in 5 HS patients led to >50% improvement in 4.

Emerging data on the efficacy of biologics as monotherapy do not fulfill the initial expectations and barely reach 50%. The efficacy of infliximab seems transient and is associated with significant toxicity as long-term treatment.

Oral isotretinoin is ineffective in the treatment of HS. In a study with 358 HS patients interviewed and examined for the effect of previous treatment with oral isotretinoin only 16.1% declared an improvement.

Wide excision remains the mainstay of therapy in extensive HS forms. Ultrasonography can identify the true extent of lesions in HS, which may be of use in preoperative planning. A study with 200 patients has shown that enclosure of gentamicin after primary excision of HS lesions can reduce the number of complications one week postoperatively but it was ineffective on the long-term recurrence rate.

LONG-TERM EFFICACY AND SAFETY RESULTS (52 WEEKS) OF A DOUBLE-BLIND, PLACEBO-CONTROLLED, CROSSOVER TRIAL OF INFlixIMAB FOR PATIENTS WITH MODERATE TO SEVERE HIDRADENITIS SUPPURATIVA
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This is a prospective, randomized, double-blind, placebo-controlled, parallel design Phase 2 study. Patients were randomized to treatment with either Infliximab 5 mg/kg or placebo on weeks 0, 2 and 6. After week 8, each patient’s treatment was unblinded and patients randomized to placebo were eligible to receive infliximab 5 mg/kg given as an induction regimen at week 8, 10 and 14 followed by a maintenance regimen of 5 mg/kg every 8 weeks. Patients randomized to infliximab continued to receive infliximab on an every 8 week schedule at weeks 14 and 22. Patients received a maximum of five infusions of infliximab. All patients were followed off therapy for and additional 22 weeks. Patients receiving Infliximab showed a dramatic response as measured by the Hidradenitis Suppurativa Severity Index (HSSI). Patient also demonstrated improvement in quality of life parameters as measured with standard DLQI.

This Clinical study represents the first formal assessment of the safety and efficacy of Infliximab treatment in moderate to severe Hidradenitis Suppurativa. Furthermore in this Phase II Trial, Infliximab was well tolerated and improvement in pain intensity, disease severity and quality of life were demonstrated.
Challenges in hidradenitis suppurativa surgery
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Hidradenitis suppurativa (HS) alias acne inversa is a challenging disease both for patients and physicians. Not only the exact etiology is still poorly understood, but also an optimal treatment modality has not been achieved until today. Actually, surgery presents the method of choice, however it is not clear whether all stages of HS should be operated in a radical manner (e.g. initial formation of open comedones). If extensive HS is present, radical surgery is necessary, however, the closure of defects is also a challenge, as a variety of methods have been described in the literature without specifying a gold standard (e.g. healing by secondary intention, split-skin, flap).

In summary the dermatologic surgeon is confronted with numerous challenges in HS surgery. The concept of HS in the Dermatologic Surgery Unit of the Ruhr-University Bochum, Germany is presented.

Treatment of hidradenitis suppurativa with a macroscopically controlled scanner-assisted carbon dioxide laser surgical technique
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The chronic fistulating lesions of hidradenitis suppurativa spread by contiguous growth, and all affected tissue needs to be surgically removed. Wide excisions, well beyond the clinical borders of activity, are mandatory, regardless of the location of hidradenitis suppurativa.

We present a macroscopically controlled scanner-assisted carbon dioxide laser surgical technique for hidradenitis suppurativa combining complete radical ablation of diseased tissue with preservation of healthy skin tissue.

The rapid-beam microprocessor-controlled optomechanical scanner system uses parallel mirrors to produce a fine spiral beam with an extremely short laser exposure time, abating tissue with minimum thermal injury. When set at the continuous mode, the scanned laser beam drills downward into the tissues and removes the lesion rapidly in an even and controlled manner. This provides a bloodless operating field, which permits macroscopic examination of the pathologic features of the tissue. The main aim is to attempt to maintain a majority of the uninvolved tissue with appropriate surgical margins or radicality and thus provide a better chance of cure and a smaller defect that can result in a lesser scar.

The wound, left to heal by secondary intention is covered by dressings that are initially left on for 2 or 3 days without changing to prevent early bleeding. Thereafter, the wound is cleaned and rinsed with tap water, and the bandage is changed as often as necessary until complete healing in four to six weeks. The scanner-assisted carbon dioxide laser surgical technique is a safe and rapid surgical method with satisfactory cosmetic and functional results suitable for use on an outpatient basis.

Neutrophilic food allergy-based treatment of hidradenitis suppurativa
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Based on my work on cellular immune cross-reactive antigen recognition at the Derm Branch of the NIH 30 years ago, I have focused my practice on searching for cross reactive stimuli of inflammatory targets manifesting as skin disorders. I do so addressing food, the largest source of antigen entering the body through the gut. In doing so, I use digestive enzymes to aid digestion, and reduce yeast and other microbes which contribute to antigenic translocation through the gut wall. This regimen has helped over half of my acne patients, and it provided significant benefit to my HS patient.

Encouraged by HS blogs telling of improvement with restriction of allergenic foods, and the story of another patient who told of clearing on a strict vegetable juice diet, I requested food allergy testing on my patient using a neutrophil enlargement/degranulation assay. She reported that her condition has cleared after eliminating the foods which tested positive on the neutrophil assay, despite the difficulty of eliminating favorites such as garlic and olive oil. Neutrophil hyperactive free radical generation has been reported as a response to phorbol myristate acetate in a limited study. Excessive neutrophil responses may lead to the massive tissue destruction seen in HS as compared to acne. Since different immune mechanisms are involved in the different forms of food allergy testing, it is just possible that the neutrophil enlargement assay provides the most pertinent data related to HS. This preliminary finding fits well enough with other limited data to suggest further exploration of this gut antigen centered approach.

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